INVENTOR SEARCH

=> d ibib abs hitstr l11 1-6

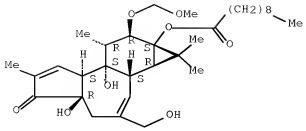
L11 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1157380 HCAPLUS Full-text
DOCUMENT NUMBER: 144:31978
TITLE: Novel phorbol esters exert dichotomous effects on inhibition of HIV-1 infection and activation of latent HIV-1 expression
AUTHOR(S): Zhong, Yu; Matsuya, Yuji; Nemoto, Hideo; Mori, Masao; Saito, Haruo; Yamamoto, Naoki
CORPORATE SOURCE: Department of Molecular Virology, Bio-Response, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan
SOURCE: Antiviral Chemistry & Chemotherapy (2005), 16(5), 303-313
CODEN: ACCHEH; ISSN: 0956-3202
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two new phorbol esters, NPB-11 (12-O- methoxymethylphorbol-13-decanoate) and NPB-15 (12-O- benzyloxymethylphorbol-13-decanoate) were synthesized. The compds. exhibited potent anti-HIV-1 activity and low cytotoxicity in MT-4 cells by MTT assay even at a high concentration [50% cytotoxic concns. (CC50) were 8.32 and 4.39 μg/mL, resp.]. Two inhibitors strongly suppressed HIV-1 (IIIB strain) replication in MT-4 cells with a 50% effective concentration (EC50) of 1.3 and 0.27 ng/mL, resp. NPB-11 efficiently blocked replication of both X4 and R5 HIV-1 in PHA-activated peripheral blood mononuclear cells and MT-4 cells as revealed by p24 assay. The antiviral activity appeared to be mediated, at least partially, by the down-regulation of the expression of CD4 and the HIV-1 co-receptors, CXCR4 and CCR5. The compds. were also capable of selectively up-regulating HIV-1 expression in a variety of latently infected cell lines and inducing cell death in HIV-1 infected cells. The effect of NPBs on the induction of HIV-1 was specifically blocked by nontoxic doses of a protein kinase C blocker, staurosporine. NPB-11 blocked the spread of HIV-1 released from latently infected ACH-2 cells to MT-4 cells in a co-culture system. When combined with AZT, NPB-11 synergistically inhibited HIV-1 replication in MTT assay using MT-4 cells. These data suggest that these agents might be useful in reducing persistent viral reservoirs in patients and as adjuvant therapy in patients treated with HAART.

IT 800385-91-5, NPB 11
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel phorbol esters exert dichotomous effects on inhibition of HIV-1 infection and activation of latent HIV-1 expression)

RN 800385-91-5 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-9-(methoxymethoxy)-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

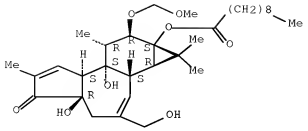
L11 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:520769 HCAPLUS Full-text
DOCUMENT NUMBER: 143:145807
TITLE: Synthesis of new phorbol derivatives having ethereal side chain and evaluation of their anti-HIV activity
AUTHOR(S): Matsuya, Yuji; Yu, Zhong; Yamamoto, Naoki; Mori, Masao; Saito, Haruo; Takeuchi, Makoto; Ito, Mamiko; Nemoto, Hideo
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Toyama, 930-0914, Japan
SOURCE: Bioorganic & Medicinal Chemistry (2005), 13(14), 4383-4388
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:145807

AB Several new phorbol derivs. having ethereal substituents at the 12-position were synthesized and subjected to biol. evaluation to find new candidates of an anti-HIV agent. Among them, 12-O-(methoxymethyl) phorbol 13-decanoate showed potent inhibitory activity against infection of HIV-1 in MT-4 cells (EC50: 1.3 ng/mL) and relatively low cytotoxicity (CC50: 8.3 μg/mL). This compound was also found to have sufficient stability in mouse plasma compared with the corresponding 12-acetate derivative, which was an equipotent HIV-1 inhibitor, but with an activity that decreased considerably after plasma treatment.

IT 800385-91-5P 800385-92-6P 800385-94-8P
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of new phorbol derivs. having ethereal side chain and evaluation of their anti-HIV activity)

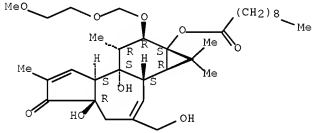
RN 800385-91-5 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-9-(methoxymethoxy)-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



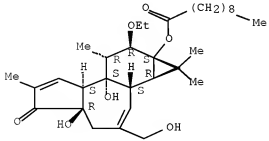
RN 800385-92-6 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-9-[(2-methoxyethoxy)methoxy]-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 800385-94-8 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-9-ethoxy-1,1a,1b,4,4a,5,7a,7b,8,9-decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (CA INDEX NAME)

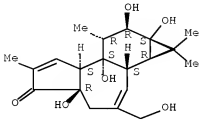
Absolute stereochemistry.



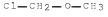
IT 17673-25-5, Phorbol
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(synthesis of new phorbol derivs. having ethereal side chain and evaluation of their anti-HIV activity)
RN 17673-25-5 HCAPLUS

CN 5H-Cyclopropa[3,4]benz[1,2-e]azulen-5-one,
1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b,9,9a-tetrahydroxy-3-
(hydroxymethyl)-1,1,6,8-tetramethyl-, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-
(CA INDEX NAME)

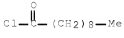
Absolute stereochemistry.



IT 107-30-2 112-13-0, Decanoyl chloride
425-75-2 3970-21-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of new phorbol derivs. having ethereal side chain
and evaluation of their anti-HIV activity)
RN 107-30-2 HCAPLUS
CN Methane, chloromethoxy- (CA INDEX NAME)

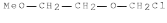


RN 112-13-0 HCAPLUS
CN Decanoyl chloride (CA INDEX NAME)



RN 425-75-2 HCAPLUS
CN Methanesulfonic acid, 1,1,1-trifluoro-, ethyl ester (CA INDEX NAME)

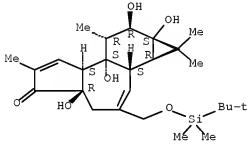
RN 3970-21-6 HCAPLUS
CN Ethane, 1-(chloromethoxy)-2-methoxy- (CA INDEX NAME)



IT 800385-85-7P, 20-O-(tert-Butyldimethylsilyl)phorbol
800385-86-8P, 20-O-(tert-Butyldimethylsilyl)phorbol
13-decanoate 800385-87-9P 800385-88-0P
800385-90-4P, 12-O-Ethyl-20-O-(tert-butyldimethylsilyl)
phorbol 13-decanoate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of new phorbol derivs. having ethereal side chain and evaluation of their anti-HIV activity)

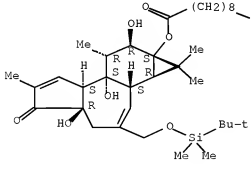
RN 800385-85-7 HCAPLUS
CN 5H-Cyclopropa[3,4]benz[1,2-e]azulen-5-one, 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b,9,9a-tetrahydroxy-1,1,6,8-tetramethyl-, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)- (CA INDEX NAME)

Absolute stereochemistry.



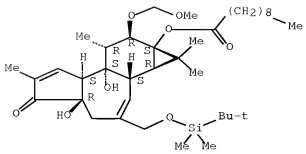
RN 800385-86-8 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b,9-trihydroxy-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



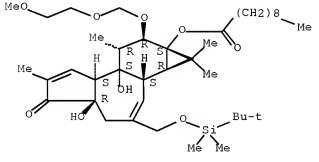
RN 800385-87-9 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-9-(methoxymethoxy)-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



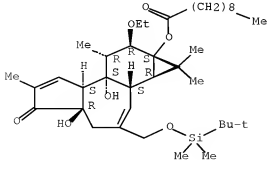
RN 800385-88-0 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,5,7a,7b,8,9-decahydro-4a,7b-dihydroxy-9-[(2-methoxyethoxy)methoxy]-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (CA INDEX NAME)

Absolute stereochemistry.



RN 800385-90-4 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-9-ethoxy-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



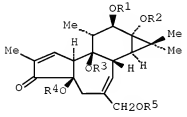
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD

(4 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1036894 HCAPLUS Full-text
DOCUMENT NUMBER: 142:16778
TITLE: Compounds and preparations having antiviral effect
INVENTOR(S): Mori, Masao; Saito, Haruo; Nemoto, Hideo; Yamamoto, Naoki; Hattori, Masao
PATENT ASSIGNEE(S): Lead Chemical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103360	A1	20041202	WO 2003-JP6422	20030522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003242405	A1	20041213	AU 2003-242405	20030522
US 20070066684	A1	20070322	US 2005-557922	20051222

PRIORITY APPLN. INFO.: WO 2003-JP6422 A 20030522
OTHER SOURCE(S): MARPAT 142:16778
GI



I

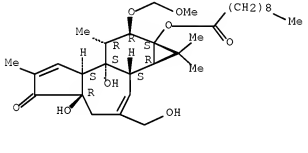
AB Antiviral prepns. containing, as the active ingredient, phorbol derivs. which are represented by the following general formula I: wherein R1 represents -CH2aX(CH2)bCH3, -CH2cX(CH2)dYCH3, -CO(CH2)eCH3or -(CH2)fCH3; R2 represents -CO(CH2)nCH3; and R3, R4 and R5 represent each hydrogen or aliphatic or aromatic carboxylate (wherein X and Y are each O or S; and a to f and n stand for each a numerical value); and show a specific safety index S.I. = EC50/EC50 (i.e., a ratio of the concentration at which HIV-1-induced cytopathogenic

effect (CPE) in MT-4 cells is inhibited by 50% to the concentration at which the survival of MT-4 cells is lowered by 50% in a cell proliferation test) of 10 or more. These prepns. are efficacious particularly against human immunodeficiency virus (HIV).

IT 800385-91-5P 800385-92-6P 800385-93-7P
800385-94-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phorbol compds. and prepns. having antiviral effect against HIV)

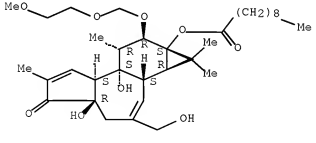
RN 800385-91-5 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-9-(methoxymethoxy)-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



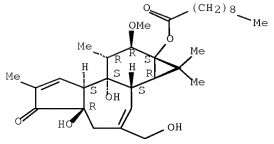
RN 800385-92-6 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-9-[(2-methoxyethoxy)methoxy]-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



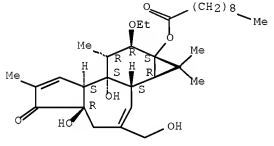
RN 800385-93-7 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-9-methoxy-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

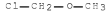


RN 800385-94-8 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-9-ethoxy-1,1a,1b,4,4a,5,7a,7b,8,9-decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (CA INDEX NAME)

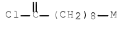
Absolute stereochemistry.



IT 107-30-2 112-13-0, Decanoyl chloride
333-27-7 425-75-2 3970-21-6
17673-25-5, Phorbol 18162-48-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(phorbol compds. and prepns. having antiviral effect against HIV)
RN 107-30-2 HCAPLUS
CN Methane, chloromethoxy- (CA INDEX NAME)



RN 112-13-0 HCAPLUS
CN Decanoyl chloride (CA INDEX NAME)



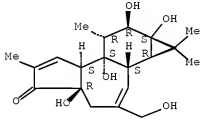
RN 333-27-7 HCAPLUS
CN Methanesulfonic acid, 1,1,1-trifluoro-, methyl ester (CA INDEX NAME)

RN 425-75-2 HCAPLUS
CN Methanesulfonic acid, 1,1,1-trifluoro-, ethyl ester (CA INDEX NAME)

RN 3970-21-6 HCAPLUS
CN Ethane, 1-(chloromethoxy)-2-methoxy- (CA INDEX NAME)

RN 17673-25-5 HCAPLUS
CN 5H-Cyclopropa[3,4]benz[1,2-e]azulen-5-one,
1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b,9,9a-tetrahydroxy-3-(hydroxymethyl)-1,1,6,8-tetramethyl-, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-
(CA INDEX NAME)

Absolute stereochemistry.



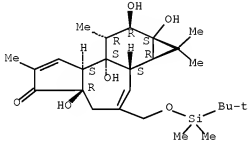
RN 18162-48-6 HCAPLUS
CN Silane, chloro(1,1-dimethylethyl)dimethyl- (CA INDEX NAME)

IT 800385-85-7P 800385-86-8P 800385-87-9P

800385-88-0P 800385-89-1P 800385-90-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(phorbol compds. and prepns. having antiviral effect against HIV)

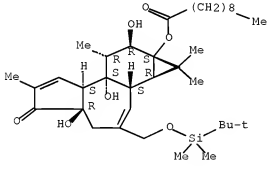
RN 800385-85-7 HCAPLUS
CN 5H-Cyclopropa[3,4]benz[1,2-e]azulen-5-one, 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b,9,9a-tetrahydroxy-1,1,6,8-tetramethyl-, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)- (CA INDEX NAME)

Absolute stereochemistry.



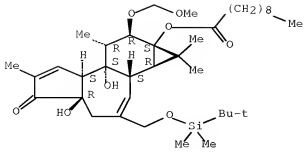
RN 800385-86-8 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b,9-trihydroxy-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



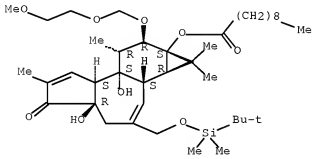
RN 800385-87-9 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-9-(methoxymethoxy)-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



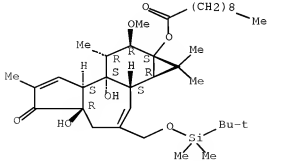
RN 800385-88-0 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,5,7a,7b,8,9-decahydro-4a,7b-dihydroxy-9-[(2-methoxyethoxy)methoxy]-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (CA INDEX NAME)

Absolute stereochemistry.



RN 800385-89-1 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,5,7a,7b,8,9-decahydro-4a,7b-dihydroxy-9-methoxy-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (CA INDEX NAME)

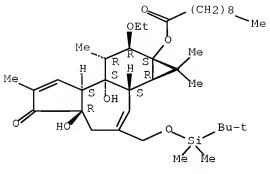
Absolute stereochemistry.



RN 800385-90-4 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-

dimethylethyl)dimethylsilyl]oxy]methyl]-9-ethoxy-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:469727 HCAPLUS Full-text
DOCUMENT NUMBER: 138:32788
TITLE: Inhibition of cytopathic effect of human immunodeficiency virus type-1 by various phorbol derivatives
AUTHOR(S): El-Mekkawy, Sahar; Meselhy, Meselhy Ragab; Abdel-Hafez, Atef Abdel-Monem; Nakamura, Norio; Hattori, Masao; Kawahata, Takuya; Otake, Toru
CORPORATE SOURCE: Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, Toyama, 930-0194, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2002), 50(4), 523-529
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:32788

AB Forty-eight derivs. of phorbol (9) and isophorbol (14) were evaluated for their inhibition of human immunodeficiency virus (HIV)-1 induced cytopathic effects (CPE) on MT-4 cells, as well as their activation of protein kinase C (PKC), as indexes of anti-HIV-1 and tumor promoting activities, resp. Of these compds., the most potent inhibition of CPE was observed in 12-O-tetradecanoylphorbol 13-acetate (8) and 12-O-acetylphorbol 13-decanoate (6). The former also showed the strongest PKC activation activity, while the latter showed no activity at 10 ng/mL. Both activities were generally observed in those phorbol derivs. with an A/B trans configuration, but not in the isophorbol derivs. with an A/B cis configuration. Acetylation of 20-OH in the phorbol derivs. significantly reduced the inhibition of CPE, as shown in 12-O-, 20-O-diacetylphorbol 13-decanoate (6a) (IC100 = 15.6 μg/mL) vs. compound 6 (IC100 = 0.0076 μg/mL), and 12-O- tetradecanoylphorbol 13,20-diacetate (8a) (IC100 = 15.6 μg/mL) vs. 12-O-tetradecanoylphorbol 13-acetate (8) (IC100 = 0.00048 μg/mL), except in the case of 12-O-decanoylphorbol 13-(2-methylbutyrate) (4) and phorbol 12,13-diacetate (9c). The reduction of a carbonyl group at C-3 abruptly reduced the inhibition of CPE, as observed in

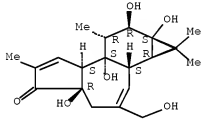
3β-hydroxyphorbol 12,13,20-triacetate (9f) (IC100 = 500 μg/mL) vs. phorbol 12,13,20-triacetate (9d) (IC100 = 62.5 μg/mL). Although 8 was equipotent in the inhibition of CPE, and activation of PKC, both activities were abruptly decreased by the acetylation of 20-OH and methylation of 4-OH [as in 8a and 4-O-methyl-12-O-tetradecanoylphorbol 13,20-diacetate (8b), resp.]. On the other hand, its positional isomer 12-O- acetylphorbol 13-tetradecanoate (8c) showed neither activities. The removal of a long acyl group in 8 led to a substantial loss of both activities, as shown in phorbol 13-acetate (9b). Of the 12-O-acetyl-13-O-acylphorbol derivs., the highest inhibition of CPE was observed in 6, which has a dodecanoyl residue at C-13. Both an increase and decrease in the number of fatty acid carbon chains resulted in significant reduction of the inhibition of CPE.

IT 17673-25-5P, Phorbol
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(phorbol and isophorbol derivs. preparation and structure-related inhibition of HIV-1-induced cytopathic effect and PKC activation)

RN 17673-25-5 HCAPLUS

CN 5H-Cyclopropa[3,4]benz[1,2-e]azulen-5-one, 1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b,9,9a-tetrahydroxy-3-(hydroxymethyl)-1,1,6,8-tetramethyl-, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-(CA INDEX NAME)

Absolute stereochemistry.

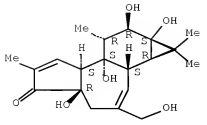


IT 17673-25-5DP, Phorbol, derivs.
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phorbol and isophorbol derivs. preparation and structure-related inhibition of HIV-1-induced cytopathic effect and PKC activation)

RN 17673-25-5 HCAPLUS

CN 5H-Cyclopropa[3,4]benz[1,2-e]azulen-5-one, 1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b,9,9a-tetrahydroxy-3-(hydroxymethyl)-1,1,6,8-tetramethyl-, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-(CA INDEX NAME)

Absolute stereochemistry.



IT 112-13-0, Decanoyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(phorbol and isophorbol derivs. preparation and structure-related inhibition of HIV-1-induced cytopathic effect and PKC activation)
RN 112-13-0 HCAPLUS
CN Decanoyl chloride (CA INDEX NAME)

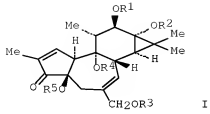
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:816455 HCAPLUS Full-text
DOCUMENT NUMBER: 135:348871
TITLE: Antiviral compositions containing phorbol derivatives as the main active ingredient
INVENTOR(S): Hattori, Masao; Yamamoto, Naoki; Mori, Masao
PATENT ASSIGNEE(S): Lead Chemical Co., Ltd, Japan
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082927	A1	20011108	WO 2000-JP2913	20000502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			WO 2000-JP2913	20000502

OTHER SOURCE(S): MARPAT 135:348871

GI



I

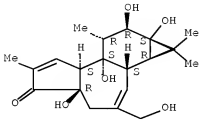
AB Described are antiviral compns. containing as the active ingredients: (i) phorbol derivs. which are represented by the general formula (I; wherein R1, R2, R3, R4 and R5 independently represent each hydrogen, an aliphatic carboxylate or an aromatic carboxylate.), have a ratio r = CC0/IC100 of 2 or more (wherein IC100 represents the concentration at which the cell pathogenic effect (CPE) of HIV-1 in MT-4 cells is inhibited at a ratio of 100; and CC0 represents the concentration at which the survival of MT-4 cells is reduced in a cell proliferation test), and show activation of protein kinase C (PKC) at a concentration of 10 ng/mL by 30% or less; and (ii) a chemical capable of suppressing or inhibiting the replication process or the maturation process of viruses. These compns. are efficacious particularly against human immunodeficiency virus (HIV). Thus, Croton tiglium seeds (3 kg) was refluxed with MeOH (10 L + 3) and the combined methanol solution was concentrated under reduced pressure to give an oil (763 g) which was suspended in 90% aqueous MeOH (7 L) and extracted with hexane (4 L + 3) and then with ether (4 L + 3). The combined ether extract was concentrated to give a resin-like substance (150 g) which was subjected to silica gel chromatog. and medium pressure liquid chromatog. to give 13-O- tigloylphorbol-20-(9Z,12Z-octadecadienoate) 60, 13-O- acetylphorbol-20-(9Z,12Z-octadecadienoate) 153, 12-O-dodecanoylphorbol-13-(2-methylbutyrate) 21, 12-O-(2-methylbutyroyl)phorbol-13-dodecanoate 30, 12-O- acetylphorbol-13-tiglate 35, 12-O-acetylphobol-13-decanoate 74, 12-O-decanoylphorbol-13-(2-methylbutyrate) 57, 12-O-tigloylphorbol-13-(2-methylbutyrate) 12, and 12-O- tetradecanoylphorbol-13-acetate 110 mg. Derivatization of these compds. by saponification, selective hydrolysis, esterification with acetic anhydride, benzoyl chloride, or butyryl chloride, reduction, or methylation, etc. gave phorbol, isophorbol, 4-deoxy-4α- phorbol, 13-O-acetylphorbol, phorbol -12,13-diacetate, 13-O-acetylcrotophorbolone-enol-20-linoleate, 12-O-tetradecanoylphorbol-13,20-diacetate, 4α- phorbol-12,13,20-triacetate, 4α-phorbol -4,12,13,20-tetraacetate, phorbol-12,13,20-triacetate, lumiphorbol-12,13,20-triacetate, 3-deoxo-3β- hydroxyphorbol-12,13,20-triacetate, 4-O-methylphorbol -12,13,20-triacetate, phorbol-4,9,12,13,20-pentaacetate, phorbol-12,13,20-tribenzoate, and 4α-phorbol -12,13,20-tributyrate. In assays for testing anti-HIV activity and PKC activation activity, 12-O-acetylphobol-13-decanoate showed IC100 and CC0 (defined as above) of 0.0076 and 62.5, resp., with r ratio of 8,220 and exhibited 0 and 17% PKC activation at 10 ng/mL and 17 μg/mL, resp.

IT 17673-25-5P, Phorbol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiviral compns. against HIV-1 containing phorbol derivs. of Croton tiglium and their derivs. as active ingredients)

RN 17673-25-5 HCAPLUS

CN 5H-Cyclopropa[3,4]benz[1,2-e]azulen-5-one, 1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b,9,9a-tetrahydroxy-3-(hydroxymethyl)-1,1,6,8-tetramethyl-, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-(CA INDEX NAME)

Absolute stereochemistry.

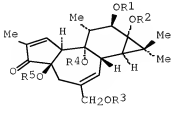


OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:369687 HCAPLUS Full-text
DOCUMENT NUMBER: 134:361358
TITLE: Phorbol derivatives as antiviral agents against HIV-1
INVENTOR(S): Hattori, Masao
PATENT ASSIGNEE(S): Lead Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001139468	A	20010522	JP 1999-320967	19991111
US 6268395	B1	20010731	US 2000-563499	20000503
PRIORITY APPLN. INFO.:			JP 1999-320967 A	19991111

GI



I

AB Phorbol derivs. (I; R1, R2, R3, R4 = H, aliphatic carboxylic acid residue or aromatic carboxylic acid residue) are claimed as antiviral agents against HIV-1 in MT-4 cells, with protein kinase C-activating actions. I were purified

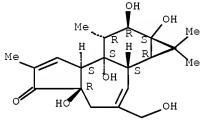
from Croton tiglium seeds or synthesized, and their antiviral actions and effects on protein kinase C activity were tested.

IT 17673-25-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phorbol derivs. as antiviral agents against HIV-1)

RN 17673-25-5 HCAPLUS

CN 5H-Cyclopropa[3,4]benz[1,2-e]azulen-5-one, 1,1a,1b,4,4a,7a,7b,8,9,9a-decahydro-4a,7b,9,9a-tetrahydroxy-3-(hydroxymethyl)-1,1,6,8-tetramethyl-, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-(CA INDEX NAME)

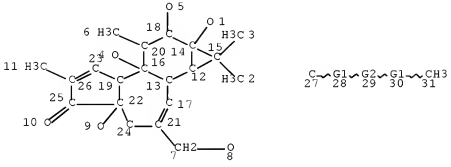
Absolute stereochemistry.



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

RESULTS FROM SEARCHES IN REGISTRY AND CAPLUS

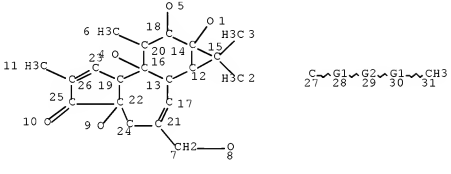
=> d que stat l37
L21 STR



VAR G1=S/O
REP G2=(1-3) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE
L23 7 SEA FILE=REGISTRY SSS FUL L21
L25 STR

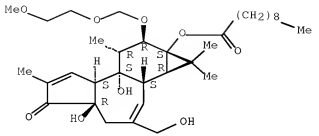


VAR G1=S/O
REP G2=(0-5) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 31

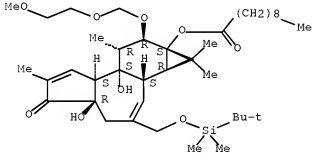
STEREO ATTRIBUTES: NONE

```
L27          7 SEA FILE=REGISTRY SSS FUL L25
L28          7 SEA FILE=REGISTRY ABB=ON  L23 OR L27
L29          3 SEA FILE=HCAPLUS ABB=ON  L28
L30          2 SEA FILE=HCAPLUS ABB=ON  L29 AND (HIV-1 OR CPE OR MT-4)
L31          3 SEA FILE=HCAPLUS ABB=ON  L29 OR L30
L32          1 SEA FILE=HCAPLUS ABB=ON  L31 AND (?SAFETY?(W)?INDEX? OR SI OR
               S.I.)
L33          3 SEA FILE=HCAPLUS ABB=ON  L31 OR L32
L34          1 SEA FILE=HCAPLUS ABB=ON  L33 AND (?CYTOPATHOGEN? OR CELL?(W)?PR
               OLIF?)
L35          3 SEA FILE=HCAPLUS ABB=ON  L33 OR L34
L36          1 SEA FILE=HCAPLUS ABB=ON  L35 AND (PRD<20030522 OR PD<20030522)
L37          3 SEA FILE=HCAPLUS ABB=ON  L35 OR L36


=> d ibib abs hitstr l37 1-3

L37  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2005:520769  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:145807
TITLE:                    Synthesis of new phorbol derivatives having ethereal
                          side chain and evaluation of their anti-HIV activity
AUTHOR(S):                Matsuya, Yuji; Yu, Zhong; Yamamoto, Naoki; Mori,
                          Masao; Saito, Haruo; Takeuchi, Makoto; Ito, Mamiko;
                          Nemoto, Hideo
CORPORATE SOURCE:         Faculty of Pharmaceutical Sciences, Toyama Medical and
                          Pharmaceutical University, Toyama, 930-0914, Japan
SOURCE:                   Bioorganic & Medicinal Chemistry (2005), 13(14),
                          4383-4388
                          CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER:                Elsevier Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
OTHER SOURCE(S):          CASREACT 143:145807
AB    Several new phorbol derivs. having ethereal substituents at the 12-position
      were synthesized and subjected to biol. evaluation to find new candidates of
      an anti-HIV agent.  Among them, 12-O-(methoxymethyl)phorbol 13-decanoate
      showed potent inhibitory activity against infection of HIV-1 in MT-4 cells
      (EC50: 1.3
      ng/mL) and relatively low cytotoxicity (CC50: 8.3 μg/mL).  This compound was
      also found to have sufficient stability in mouse plasma compared with the
      corresponding 12-acetate derivative, which was an equipotent HIV -1 inhibitor,
      but with an activity that decreased considerably after plasma treatment.
IT    800385-92-6P
      RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
      activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL
      (Biological study); PREP (Preparation); USES (Uses)
         (synthesis of new phorbol derivs. having ethereal side chain and
         evaluation of their anti-HIV activity)
RN    800385-92-6  HCAPLUS
CN    Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-1,1a,1b,4,4a,5,7a,7b,9,9-
      decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-9-[(2-methoxyethoxy)methoxy]-
      1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester
      (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
```



IT 800385-88-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of new phorbol derivs. having ethereal side chain and evaluation of their anti-HIV activity)
RN 800385-88-0 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,5,7a,7b,8,9-decahydro-4a,7b-dihydroxy-9-[(2-methoxyethoxy)methoxy]-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (CA INDEX NAME)

Absolute stereochemistry.

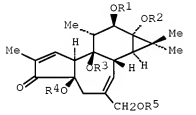


OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1036894 HCAPLUS Full-text
DOCUMENT NUMBER: 142:16778
TITLE: Compounds and preparations having antiviral effect
INVENTOR(S): Mori, Masao; Saito, Haruo; Nemoto, Hideo; Yamamoto, Naoki; Hattori, Masao
PATENT ASSIGNEE(S): Lead Chemical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004103360 A1 20041202 WO 2003-JP6422 20030522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003242405 A1 20041213 AU 2003-242405 20030522
US 20070066684 A1 20070322 US 2005-557922 20051222
PRIORITY APPLN. INFO.: WO 2003-JP6422 A 20030522
OTHER SOURCE(S): MARPAT 142:16778
GI



I

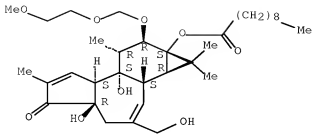
AB Antiviral prepns. containing, as the active ingredient, phorbol derivs. which are represented by the following general formula I: wherein R1 represents -CH2aX(CH2)bCH3, -CH2cX(CH2)dYCH3, -CO(CH2)eCH3or -(CH2)fCH3; R2 represents -CO(CH2)nCH3; and R3, R4 and R5 represent each hydrogen or aliphatic or aromatic carboxylate (wherein X and Y are each O or S; and a to f and n stand for each a numerical value); and show a specific safety index S.I. = EC50/EC50 (i.e., a ratio of the concentration at which HIV-1-induced cytopathogenic effect (CPE) in MT-4 cells is inhibited by 50% to the concentration at which the survival of MT-4 cells is lowered by 50% in a cell proliferation test) of 10 or more. These prepns. are efficacious particularly against human immunodeficiency virus (HIV).

IT 800385-92-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phorbol compds. and prepns. having antiviral effect against HIV)

RN 800385-92-6 HCAPLUS

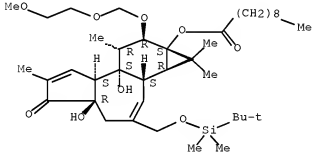
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-1,1a,1b,4,4a,5,7a,7b,9,9-decahydro-4a,7b-dihydroxy-3-(hydroxymethyl)-9-[(2-methoxyethoxy)methoxy]-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



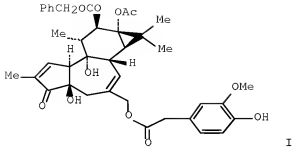
IT 800385-88-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(phorbol compds. and prepns. having antiviral effect against HIV)
RN 800385-88-0 HCAPLUS
CN Decanoic acid, (1aR,1bS,4aR,7aS,7bS,8R,9R,9aS)-3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,1a,1b,4,4a,5,7a,7b,8,9-decahydro-4a,7b-dihydroxy-9-[(2-methoxyethoxy)methoxy]-1,1,6,8-tetramethyl-5-oxo-9aH-cyclopropa[3,4]benz[1,2-e]azulen-9a-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:422512 HCAPLUS Full-text
DOCUMENT NUMBER: 125:114883
ORIGINAL REFERENCE NO.: 125:21579a,21582a
TITLE: Synthesis and Evaluation of Phorboid 20-Homovanillates: Discovery of a Class of Ligands Binding to the Vanilloid (Capsaicin) Receptor with Different Degrees of Cooperativity
AUTHOR(S): Appendino, Giovanni; Cravotto, Giancarlo; Palmisano, Giovanni; Annunziata, Rita; Szallasi, Arpad
CORPORATE SOURCE: Dipartimento di Scienza e Tecnologia del Farmaco, Universita Degli Studi di Torino, Turin, 10125, Italy
SOURCE: Journal of Medicinal Chemistry (1996), 39(16), 3123-3131
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

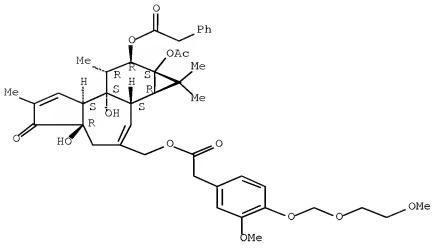
AB A number of phorboid 20-homovanillates were prepared by condensation of phorbol 12,13-diesters and 12-dehydrophorbol 13-esters with Mem-homovanillic acid followed by removal of the protecting group with SnCl4 in THF. These compds. were evaluated for their ability to inhibit [3H]resiniferatoxin (RTX) binding to rat spinal cord membranes. Compds. bearing a lipophilic ester group on ring C were considerably active, but a surprising tolerance of the vanilloid receptor toward the location and the orientation of this ester group was disclosed. Unexpectedly, these ligands could also diminish, to a variable degree, the pos. cooperativity which characterizes RTX binding to the vanilloid receptor. Phorbol 12-phenylacetate 13-acetate 20-homovanillate (PPAHV, I), a compound which abolished binding cooperativity, was further tested in a variety of in vivo assays used to characterize vanilloid-like activity. PPAHV showed only a marginal pungency and failed to induce a measurable hypothermia response at doses (up to 200 mg/kg) at which it effectively desensitized against neurogenic inflammation. These data suggest that the peculiar binding behavior of these ligands might be associated with a distinct spectrum of biol. activity.

IT 179258-46-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and evaluation of phorboid 20-homovanillates as ligands binding to vanilloid (capsaicin) receptor with different degrees of cooperativity)

RN 179258-46-9 HCAPLUS

CN Benzeneacetic acid, 3-methoxy-4-[(2-methoxyethoxy)methoxy]-, [9a-(acetyloxy)-1a,1b,4,4a,5,7a,7b,8,9,9a-decahydro-4a,7b-dihydroxy-1,1,6,8-tetramethyl-5-oxo-9-[(phenylacetyl)oxy]-1H-cyclopropa[3,4]benz[1,2-e]azulen-3-yl]methyl ester, [1aR-(1aα,1bβ,4aβ,7aα,7bα,8α,9β,9a.alpha.)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 33 THERE ARE 33 CAPLUS RECORDS THAT CITE THIS RECORD (33 CITINGS)

SEARCH HISTORY

```
=> d his ful

     (FILE 'HOME' ENTERED AT 13:25:20 ON 20 OCT 2009)

     FILE 'HCAPLUS' ENTERED AT 13:25:37 ON 20 OCT 2009
                E MORI MASAO/AU
L1          151 SEA ABB=ON  "MORI MASAO"/AU
                E SAITO HARUO/AU
L2          316 SEA ABB=ON  "SAITO HARUO"/AU
                E NEMOTO HIDEO/AU
L3          279 SEA ABB=ON  "NEMOTO HIDEO"/AU
                E YAMAMOTO NAOIKI/AU
L4          134 SEA ABB=ON  ("YAMAMOTO NAOICHI"/AU OR "YAMAMOTO NAOICHIRO"/AU
                OR "YAMAMOTO NAOIKI"/AU OR "YAMAMOTO NAOJCHI"/AU)
                E HATTORI MASAO/AU
L5          439 SEA ABB=ON  "HATTORI MASAO"/AU
L6            0 SEA ABB=ON  L1 AND L2 AND L3 AND L4 AND L5
L7         1297 SEA ABB=ON  L1 OR L2 OR L3 OR L4 OR L5
L8           45 SEA ABB=ON  L7 AND "ANTIVIRAL"
L9            7 SEA ABB=ON  L8 AND ?PHORBOL?
                SELECT RN L9 3

     FILE 'REGISTRY' ENTERED AT 13:27:24 ON 20 OCT 2009
L10          17 SEA ABB=ON  (107-30-2/BI OR 112-13-0/BI OR 17673-25-5/BI OR
                18162-48-6/BI OR 333-27-7/BI OR 3970-21-6/BI OR 425-75-2/BI OR
                800385-85-7/BI OR 800385-86-8/BI OR 800385-87-9/BI OR 800385-88
                -0/BI OR 800385-89-1/BI OR 800385-90-4/BI OR 800385-91-5/BI OR
                800385-92-6/BI OR 800385-93-7/BI OR 800385-94-8/BI)

     FILE 'HCAPLUS' ENTERED AT 13:27:29 ON 20 OCT 2009
L11           6 SEA ABB=ON  L9 AND L10

     FILE 'REGISTRY' ENTERED AT 13:29:16 ON 20 OCT 2009
L12             STRUCTURE  17673-25-5
L13          39 SEA SSS SAM L12
L14         746 SEA SSS FUL L12
L15         548 SEA ABB=ON  L14 AND N=0

     FILE 'HCAPLUS' ENTERED AT 13:31:35 ON 20 OCT 2009
L16       15628 SEA ABB=ON  L15
L17       14030 SEA ABB=ON  L16 AND ?PHORBOL?

     FILE 'REGISTRY' ENTERED AT 13:32:45 ON 20 OCT 2009
L18             STR L12
L19           0 SEA SSS SAM L18
L20           2 SEA SSS FUL L18
L21             STR L18
L22           0 SEA SSS SAM L21
L23           7 SEA SSS FUL L21

     FILE 'HCAPLUS' ENTERED AT 13:38:04 ON 20 OCT 2009
L24           3 SEA ABB=ON  L23

     FILE 'REGISTRY' ENTERED AT 13:38:53 ON 20 OCT 2009
L25             STR L21
L26           0 SEA SSS SAM L25
```

```
L27             7 SEA SSS FUL L25
L28             7 SEA ABB=ON  L23 OR L27

     FILE 'HCAPLUS' ENTERED AT 13:40:27 ON 20 OCT 2009
L29             3 SEA ABB=ON  L28
L30             2 SEA ABB=ON  L29 AND (HIV-1 OR CPE OR MT-4)
L31             3 SEA ABB=ON  L29 OR L30
L32             1 SEA ABB=ON  L31 AND (?SAFETY?(W)?INDEX? OR SI OR S.I.)
L33             3 SEA ABB=ON  L31 OR L32
L34             1 SEA ABB=ON  L33 AND (?CYTOPATHOGEN? OR CELL?(W)?PROLIF?)
L35             3 SEA ABB=ON  L33 OR L34
L36             1 SEA ABB=ON  L35 AND (PRD<20030522 OR PD<20030522)
L37             3 SEA ABB=ON  L35 OR L36

     FILE HOME

     FILE HCAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.
     The CA Lexicon is the copyrighted intellectual property of the
     American Chemical Society and is provided to assist you in searching
     databases on STN.  Any dissemination, distribution, copying, or storing
     of this information, without the prior written consent of CAS, is
     strictly prohibited.

     FILE COVERS 1907 - 20 Oct 2009  VOL 151 ISS 17
     FILE LAST UPDATED: 19 Oct 2009  (20091019/ED)
     REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Aug 2009
     USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Aug 2009

     HCAplus now includes complete International Patent Classification (IPC)
     reclassification data for the third quarter of 2009.

     CAS Information Use Policies apply and are available at:

     http://www.cas.org/legal/infopolicy.html

     This file contains CAS Registry Numbers for easy and accurate
     substance identification.

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   18 OCT 2009  HIGHEST RN 1188905-91-0
     DICTIONARY FILE UPDATES:  18 OCT 2009  HIGHEST RN 1188905-91-0

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For information
```

on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html